

AMENDMENTS TO THE CLAIMS

Claims 2, 3, 7-10, 12, and 15-20 have been canceled. Claims 1, 4-6, 11, 13 and 14 are now pending. Claims 1, 4-6, 11, 13 and 14 have been amended as shown. This listing of claims will replace all prior versions and listings of claims in the Application.

Listing of Claims:

Claim 1 (currently amended): A method for determining that whether a human subject is at risk for developing obesity comprising ~~the steps of:~~

assaying obtaining a sample from a human subject, said sample comprising (a) a TBC1D1-encoding nucleic acid molecule or the complement thereof, or (b) a TBC1D1 protein; and

detecting a cytidine to thymidine alteration at the 373rd nucleotide of the TBC1D1 coding sequence of SEQ ID NO:1, an alteration in (a) said TBC1D1-encoding nucleic acid molecule or complement thereof, or (b) said TBC1D1 protein;

wherein the presence of said cytidine to thymidine alteration identifies the a subject as being at risk for developing obesity.

Claims 2 and 3 (cancelled)

Claim 4 (currently amended): The method of Claim 1 wherin said assaying detection step is conducted on genomic DNA encoding TBC1D1.

Claim 5 (currently amended): The method of Claim 1 wherin said assaying detection step is conducted on mRNA or cDNA encoding TBC1D1.

Claim 6 (currently amended): The method of Claim 1, wherein said cytidine to thymidine alteration nucleotide variant is detected by a method selected from the group consisting of:

- a) hybridizing a probe specific for said alteration to RNA isolated from said human sample and detecting the presence of a hybridization product, wherein the presence of said product indicates the presence of said alteration in the sample;
- b) hybridizing a probe specific for said alteration to cDNA made from RNA isolated from said sample and detecting the presence of a hybridization product, wherein the presence of said product indicates the presence of said alteration in the sample;
- c) hybridizing a probe specific for said alteration to genomic DNA isolated from said sample and detecting the presence of a hybridization product, wherein the presence of said product indicates the presence of said alteration in the sample;
- d) amplifying all or part of said TBC1D1-encoding nucleic acid molecule, or complement thereof, in said sample using a set of primers to produce amplified nucleic acids and sequencing the amplified nucleic acids;
- e) amplifying part of said TBC1D1-encoding nucleic acid molecule, or complement thereof, in said sample using a primer specific for said alteration and detecting the presence of an amplified product, wherein the presence of said product indicates the presence of said alteration in the sample;
- f) molecularly cloning all or part of said TBC1D1-encoding nucleic acid molecule, or complement thereof, in said sample to produce a cloned nucleic acid and sequencing the cloned nucleic acid;
- g) amplifying said TBC1D1-encoding nucleic acid molecule, or complement thereof, to produce amplified nucleic acids, hybridizing the amplified nucleic acids to a DNA probe specific said alteration and detecting the presence of a hybridization product, wherein the presence of said product indicates the presence of said alteration;
- h) forming single-stranded DNA from a gene fragment of said TBC1D1-encoding nucleic acid molecule, or complement thereof, from said human sample and single-stranded DNA from a corresponding fragment of a wild-type gene, electrophoresing said single-stranded DNAs on a non-denaturing polyacrylamide gel and comparing the mobility of said single-stranded DNAs on said gel to determine if said single-stranded DNA from said sample is shifted relative to wild-type and sequencing said single-stranded DNA having a shift in mobility;

- i) forming a heteroduplex consisting of a first strand of nucleic acid selected from the group consisting of a genomic DNA fragment isolated from said sample, an RNA fragment isolated from said sample and a cDNA fragment made from mRNA from said sample and a second strand of a nucleic acid consisting of a corresponding human wild-type gene fragment, analyzing for the presence of a mismatch in said heteroduplex, and sequencing said first strand of nucleic acid having a mismatch;
- j) forming single-stranded DNA from said TBC1D1-encoding nucleic acid molecule, or complement thereof, of said human sample and from a corresponding fragment of an allele specific for said alteration, electrophoresing said single-stranded DNAs on a non-denaturing polyacrylamide gel and comparing the mobility of said single-stranded DNAs on said gel to determine if said single-stranded DNA from said sample is shifted relative to said allele, wherein no shift in electrophoretic mobility of the single-stranded DNA relative to the allele indicates the presence of said alteration in said sample; and
- k) forming a heteroduplex consisting of a first strand of nucleic acid selected from the group consisting of a genomic DNA fragment of said TBC1D1-encoding nucleic acid molecule, or complement thereof, isolated from said sample, an RNA fragment isolated from said sample and a cDNA fragment made from mRNA from said sample and a second strand of a nucleic acid consisting of a corresponding gene allele fragment specific for said alteration and analyzing for the presence of a mismatch in said heteroduplex, wherein no mismatch indicates the presence of said alteration.

Claims 7 – 10 (cancelled)

Claim 11 (currently amended): The method of claim 1, wherein said assaying detection step comprises hybridizing a nucleic acid probe specifically hybridizable to an altered TBC1D1 coding sequence[.,.] or complement thereof.

Claim 12 (cancelled)

Claim 13 (currently amended): A method for predicting, in a human subject, the likelihood of developing obesity associated with a genetic variant variants of the human *TBC1D1* gene comprising detecting the presence or absence of:

detecting the presence of a cytidine to thymidine alteration at the 373rd nucleotide of the TBC1D1 coding sequence of SEQ ID NO:1, a nucleotide variant encoding

R125W, in a TBC1D1 encoding nucleic acid of said subject; or

the amino acid substitution R125W, in a TBC1D1 protein of said subject;

wherein the presence of said cytidine to thymidine alteration nucleotide variant, or said amino acid substitution, predicts that said subject has an increased likelihood of developing obesity.

Claim 14 (currently amended): The method of claim 13, wherein said cytidine to thymidine alteration nucleotide variant associated with obesity is detected by determining the genomic sequence of said TBC1D1 *TBC1D1* gene.

Claim 15 – 20 (cancelled)